05-05-05

LUD 5253.5 DIV (09885911)

1644

CERTIFICATE OF EXPRESS MAIL

"Express Mail" mailing label # EV 331564288 US

Date of Deposit May 4, 2005

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service on the date indicated above and is addressed to the Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Name of Depositor: Fani Malikouzakis

Signature of Depositor Fani Malikouzakis

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant	:	Thierry BOON-FALLEUR et al.
Serial No.	:	08/819,669
Filed	:	March 17, 1997
For	:	TUMOR REJECTION, ANTIGEN PRECURSORS, TUMOR REJECTION ANTIGENS AND USES THEREOF
Art Unit	:	1644
Examiner	:	P. Gambel

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY TO SUPPLEMENTAL EXAMINER'S ANSWER

This is in Reply to the Supplemental Examiner's Answer, dated March 11, 2005.

The Examiner is reminded that this application has been made special. A delay of 4 months in filing the Supplemental Examiner's Answer does not appear justified in view of this status.

Appellants also have to query why, after 8 years of prosecution, and a 55 page Examiner's Answer, the Examiner still has enough to say to fill 25 pages. Appellants will address the points raised in this latest paper in the order raised therein.

Appellants consider the Examiner's response to their query to the Board unresponsive, and again request the Board to address this issue. They do reiterate that, in view of 8 years of pendency, they felt that they had no choice but to agree to the new Grouping and new rejection.

Page 2 of the Supplemental Examiner's Answer is, essentially, a series of quotations from prior prosecution. All well and good, but the point is simply that the Examiner:

(i) added a new reference;

(ii) made a new rejection;

(iii) regrouped the claims.

The Examiner states at page 3, that:

> "(G)iven the absence of a definition of vaccine in the specification as filed, the Examiner introduced a dictionary definition for clarity."

The time to have done so, however, was during prosecution, not in the Examiner's Answer. Further, the reference was not added just for clarity. It was used in a new rejection.

Further, if the definition is in accordance with the "plain and ordinary meaning" of the term, appellants did not introduce any prosecution on the issue of the proper interpretation of vaccine, and there had not been any issue raised with respect to the meaning of the term during prosecution, why is this an issue now?

Appellant now wishes to turn to page 4 of the Supplemental Examiner's Answer. The Examiner asserts that the references were listed as "Art of Record" not "prior art."

The following is a quotation from page 4 of the Examiner's Answer:

> "(a) Art of Record
>
> The following is a listing of the prior art of record relied upon in the rejection of the claim on appeal."

(emphasis added). A copy of page 4 of the Examiner's Answer is appended to show this in the Evidentiary Appendix.

Appellants are entitled to make this an issue. The law on when references that are not prior art can be used is far from what the Examiner states it is. How **NON**-prior art may be applied differs from how prior art may be. This is a distinction with a difference, contrary to the Examiner's position, which seems to be that all art is equivalent.

Further, while the Examiner's candor as to the deletion of Ding is appreciated, it is pointed out that, throughout prosecution, the Examiner did in fact rely on Ding as a primary reference. If Ding is not applied then those rejections are *de facto* withdrawn, and the Examiner should so state.

At page 5, the Examiner summarizes his position. The rejection is then presented, starting at "III." Appellants will now address these issues.

WRITTEN DESCRIPTION

At the bottom of page 5, though page 6, the Examiner asserts that comments appellants made in their replay brief are misleading. The specific sentence referred to is:

> "One of ordinary skill in the art recognizes such as the molecule constitutes cDNA because cDNA contains only coding regions."

First, the sentence as presented by the Examiner is misleading, because it is not presented in context. The sentences that follow read as follows:

> "MAGE-5 is presented as SEQ ID NO: 16. It is labeled as genomic DNA, but within nucleotides 645-908, one finds the sequence presented as triplets, i.e., a coding region."

The Examiner alleges in his Answer:

> "The specification does not provide for the cDNA or amino acid sequence as well as the isolation of a MAGE tumor rejection antigen precursor protein itself for each of the 11 species of MAGE1-11 in the specification as filed."

In their reply appellants were simply pointing out that, when nucleotides are presented in triplet form, this is a signal to the skilled artisan that a protein is encoded. Each triplet stands for an amino acid and the correspondence between triplets and amino acids is well known. For example, triplet "ATG" is always the amino acid methionine, or "Met." The point that appellants were making is that by presenting triplet codons, appellants *de facto* present an amino acid sequence. If the Examiner or the Board construed appellants remarks to mean that cDNA includes only coding regions, the confusion caused by these remarks is regretted.

Returning to the Supplemental Examiner's Answer, page 6 et seq., the point the Examiner is making is not seen. The fact that a molecule is weakly expressed is irrelevant when

expression levels are not a part of the claim. The fact that a complete structure is not provided is not dispositive. In Enzo Biochem. Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002), the Court held:

> "(T)he written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

Enzo at 1324 (emphasis added).

Structure is provided in the claims, via the requirement that the encoding molecules hybridize to a relevant molecule, at specific conditions. A function is recited, i.e., that the claimed protein serve as a precursor to a peptide which stimulates T cells.

Whether MAGE-5, 8, 9, 10, and 11 were expressed weakly or strongly, is simply not relevant. They were expressed. The claims do not require a degree of expression.

Further, assuming arguendo that there is a requirement for strong expression, it appears that the Examiner accepts that MAGE-1, 2, 3, 4, and 6 are expressed strongly. Using the Examiner's faulty criterion, 5 examples are given. Using the correct criterion, the number is 10.

The Examiner invites appellants to review the "detailed analysis" of the Examiner's Answer. Appellants have done so, but defer to the facts of the case, and the relevant case law, which support appellants position.

At page 7, continuing through page 8, the Examiner now ignores a prior argument made to reject the claims. Specifically, Ding, cited *supra*, was alleged to show lack of written description and enablement because it showed MAGE molecules were polymorphic. Actually, what it showed was that the class of MAGE molecules which function as TRAPs tolerates sequence variation. Skolnick and Bork do not contradict this. These references warn about attributing functional similarity based solely on computer searches for sequence homology. Since the claims do not recite sequence homology, but other properties, the argument is irrelevant. Further, both the application and the DePlaen reference, relied upon so heavily by the Examiner, attribute similar properties to molecules within the claims, and show that the

molecules possess the properties. The "glittering generalities" made by the Examiner are simply not pertinent.

The Examiner's comments on page 9, are misleading. Appellants specifically refer to Vantomme, Zhang, Atanackovic and Krevitt for showing the TRAPs function as vaccines. The comments at the top of page 9 make no sense.

Turning to the bottom of page 9, through page 10, again the Examiner appears to be reading quantitative limitations into the claims that are not there. Further, the Examiner ignores statements such as the following, in Vantomme, et al., 131, second column:

> "The MAGE-3 vaccine was well tolerated and was associated with clinical benefit in 6/57 enrolled patients and 6/39 patients who received at least 4 vaccinations."

(emphasis added).

Of Zhang (page 224, second column):

> "Because these homologous peptides (i.e., MAGE 1, 2, 4, 6, 10 or 11), are also recognized by one of the $CD4^+$ T cell clones, we can suppose that such T cells may be activated in patients injected with the MAGE-3 peptide or a MAGE-3 protein.
>
> * * *
>
> These T cells well be able to recognize not only the MAGE-3 expressing cells, but also other tumor cells that do not express MAGE-3 or that have lost the expression of MAGE-3, provided that they express one of the other MAGE genes.

(emphasis added).

The very title of Atanackvoic, et al., "Vaccine induced $CD4^+$ T Cell Responses to MAGE-3 Protein In Lung Cancer Patients" speaks for itself, as does the Krevitt title "Phase I/II Study of Vaccination with a MAGE-3 Protein Plus Immunological Adjuvant."

The Examiner concludes that the references:

> "Support the position that 'cancer vaccines' raise additional levels of consideration under 35 U.S.C. 112, first paragraph, with respect to satisfying the characteristics of vaccine."

What the references do is show that MAGE proteins do work as vaccines, but much remains to be done to maximize their potential. Again, the Examiner seems to be reading recitations into the claims that is not present.

The Examiner then turns to U.S. Patent No. 5,405,940, and tries to impose an interpretation on it that is absolutely untenable.

All of the MAGE molecules hybridized to SEQ ID NO: 8. What '940 teaches is that, while the specific T cells stimulates may differ, they will all stimulate T cells. The claims do not require that a specific T cell will be stimulated, nor that a specific TRA be employed (at least in the first Group of claims).

It is not clear where the Examiner finds a basis for reading these requirements into the claims. The rejection appears to be based on something that is not claimed.

At page 11 of the Supplemental Examiner's Answer, the Examiner appears to agree that the specification does provide written description support for the tumor rejection antigen of SEQ ID NO: 26 - yet, in considering the claims that recite this molecule, the Examiner reiterates the written description requirement. This is not consistent. In any event, the introduction of this argument is believed to be a red herring, since most of the claims do not recite a specific tumor rejection antigen. Claims 183, 185, 186, 188, 189, and 190 do not recite a specific TRA, so the issue is moot, and claims 184, 187, and 190 require SEQ ID NO: 26, which the Examiner agrees is disclosed. Hence, the issue regarding SEQ ID NO: 26 is irrelevant, as is the issue regarding HLA binding, since specific HLA molecules are not recited. To this end, the Examiner's position at page 12 of the Supplemental Examiner's Answer simply repeats this information, and adds nothing to the dialogue.

At page 13, the Examiner raises another non-issue, i.e., the fact that the claims do not recite "stringent conditions."

It is worthwhile to review the prosecution history regarding this phrase. Appellants originally did recite the phrase "under stringent conditions" in the claims, which was permitted in the parent case, which issued as U.S. Patent No. 5,342,274. The Examiner balked at it, and rejected the claims under 35 U.S.C. § 112. In response, appellants added the present conditions, which the Examiner accepted as resolving the rejection under 35 U.S.C. § 112, and agreeing that the recitation was supported by the specification definition of "stringent conditions."

To raise subsidiary issues now, as to alleged incompleteness in the claims (see third and fourth paragraphs of page 13 of the Supplemental Examiner's Answer), is totally contrary to the spirit of prompt and expeditious prosecution, as well as the rules related to appellate practice.

Quoting extensive sections of the Examiner's Answer, and then arguing Ding (page 14 of the Supplemental Examiner's Answer), does not cure this. The fact the Ding discloses full length molecules is irrelevant, for two reasons.

First, appellants do so as well. There has been absolutely no challenge to, e.g., MAGE 1, 2, 3, 4 and 6. As there are absolutely no rules in how many species are required to satisfy the written description requirement, five should be sufficient. They all meet the criteria of the claims.

Second, as was pointed out, supra, the Federal Circuit, via the Enzo case, has clearly established that a full length nucleic acid molecule is not required for written description.

With regard to the statements made by the Examiner, on page 15, the Examiner asserts that none of the disclosed TRAPs satisfy the criteria for the molecules set forth in the claims. As has been pointed out, supra even if the Examiner were correct about several of the TRAP molecules (and he is not), the Examiner has presented nothing to challenge, e.g., MAGE1-4.

The Examiner's attempts to distinguish Example 9 of the Interim Written Description Guidelines are not persuasive. The Examiner cannot make definitive statements as to how many molecules are covered by the claims, just as the Examiner cannot say how many molecules were encompassed by Example 9 of the Guidelines. The Guidelines specifically state a genus is covered. See page 36:

> "The claim is drawn to a genus of nucleic acids, all of which must hybridize with SEQ ID NO: 1 and must encode a protein with a specific activity."

Hence, the Examiner's attempt to distinguish the Guidelines on the basis of scope, are without merit.

It is also ironic that throughout the prosecution, the Examiner "reminded" appellants of the Interim Written Description Guidelines, as if these supported his position. Now, he appears to assert they are not relevant.

The Interim Written Description Guidelines, the case law, and the facts all support appellants' position that the written description requirement of 35 U.S.C. § 112 is met. The rejection should be reversed.

At page 16 of the Supplemental Examiner's Answer, the Examiner yet again misstates appellants' remarks. Whatever the Examiner did previously, he did not treat claims to vaccines separately from all others, he did not cite the Illustrated Dictionary of Immunology, and he did not feel any need to raise issues as to the definition of a vaccine. Referring to MPEP 2111 does not change this.

The Examiner then goes on to present an argument, although it is not at all clear to what the argument refers. Two point "C"s are recited, referring to pages 38-41 and 52-55 of the Examiner's Answer, but then goes on to discuss written description, again. While the Examiner quotes Enzo Biochem, which was discussed supra, he appears to be relying on In re Wallach, 71 USPQ2d 1939 (Fed. Cir. 2004). The Examiner characterizes the Wallach holding as:

> "Because the inventors did not know the complete amino acid sequence of the protein at the time of filing their patent application, they did not possess any of the DNA sequences encoding the isolated protein."

Indeed, in Wallach the applicants were claiming nucleic acid molecules, not proteins. Further, this decision points out that, in a divisional application, claims which recited partial amino acid sequence and functionality were deemed allowable. See Wallach at 1332.

The divisional application where proteins were claimed, is more pertinent here than is the actual application under consideration by the Federal Circuit in Wallach. One learns from the Wallach decision that the protein claims recited:

(1) 10 amino acids (out of 185-192 in the total sequence);

(2) a molecular weight, and

(3) a function.

The holding of the Federal Circuit was that these three properties did not show any correlation to the structure of the DNA encoding the proteins, and this, taken with the absence of any information on DNA structures, was sufficient to deem the DNA claims to lack adequate written description.

As was pointed out supra, the claims under consideration were claims directed to DNA, not to proteins. Such is also the case here. Further, the protein claims were deemed allowable.*

The Examiner reiterated his reliance on Vas-Cath v. Mahurkar, Fiers v. Revel and Amgen Inc. v. Chugai Pharmaceuticals Company. All of these cases were discussed and distinguished by appellants. Please see page 6 et seq. of Appellants Reply Brief. As has been the case throughout this prosecution, however, the Examiner appears to feel that it is sufficient to reiterate his position, rather than to attempt to rebut arguments presented by appellants.

The Examiner then harps on the fact that a sequence was corrected during the prosecution of the application (see page 20 of the Supplemental Examiner's Answer). The fact is, there is absolutely no evidence that the error did or would impact the ability of the claimed proteins to function as TRAPs. Indeed, as the Ding reference pointed out, such disparities are inconsequential.

At page 21, the Examiner asserts that appellants have not addressed alleged deficiencies, and argues that all one has is a "mere wish or plan for obtaining the claimed invention," and again reiterates that not all of the disclosed sequences meet the criteria of MAGE TRAPs.

With all due respect, while the Examiner may not care for the answers, each and every assertion has been addressed. Further, the Examiner's position continues to be that all disclosed species must satisfy all criteria of claimed subject matter. No case law, regulation, or statute supports this position.

At page 22, the Examiner then brings in the recent decision Chiron Corp. v. Genentech, Inc., 70 USPQ2d 13121 (Fed. Cir. 2004). The Examiner misquotes Chiron Corp. The Examiner states that the Court noted (in Chiron Corp. v. Genentech):

> "we do not read Hogan as allowing an inventor to claim what was specifically desired but difficult to obtain at the time the application was filed, unless the patent discloses how to make and use it."

Actually, the Chiron court pointed out that this quotation is from an earlier case, Plant Genetics Sys N.V. v. DeKalb Genetics Corp., 313 F.3d 1335; 65 USPQ2d 1452 (Fed. Cir. 2003). The distinction that the Chiron court makes between Hogan and Plant Genetics is relevant here:

---

* Indeed, a search of PAIR reveals that the applicants have received a favorable decision in their interference.